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APPLICATION NUMBER: 60/480,208

FILING DATE: June 20, 2003

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Express Mail Label No.

EV 291442346 US

17399 U.S. PTO
60/480208

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Additional inventors are being named on the _____ separately numbered sheets attached hereto					
TITLE OF THE INVENTION (500 characters max)					
HEPATIC DEVICE FOR TREATMENT, EATING DETECTION, AND GLUCOSE LEVEL DETECTION					
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ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/>	Specification	Number of Pages	20	<input type="checkbox"/> CD(s), Number	
<input checked="" type="checkbox"/>	Drawing(s)	Number of Sheets	1	<input checked="" type="checkbox"/> Other (specify)	1. Check in the amount of \$160.00 2. Acknowledgement Postcard
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Respectfully submitted,

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[Page 1 of 2]

Date

6/20/03

REGISTRATION NO.
(if appropriate)
Docket Number:

26,723

501049.20544

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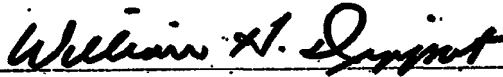
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Applicant: Offer Glasberg
Serial No: Not yet assigned
Filing Date: June 19, 2003 herewith
For: HEPATIC DEVICE FOR TREATMENT, EATING DETECTION, AND GLUCOSE LEVEL
DETECTION
Enclosures: (1) Provisional Application Cover Sheet (1 page); (2) Specification (20 pages);
(3) Drawings (1 sheet); (4) Check in the amount of \$160.00; (5) Acknowledgement postcard

HEPATIC DEVICE FOR TREATMENT, EATING DETECTION, AND GLUCOSE LEVEL DETECTION

CROSS-REFERENCE TO RELATED APPLICATION

The present patent application is related to a US Provisional Patent Application
5 entitled, "Gastrointestinal methods and apparatus for use in treating disorders," filed
on even date herewith, which is assigned to the assignee of the present application and
is incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates generally to electrical stimulation and sensing,
10 and specifically to invasive techniques and apparatus for electrical stimulating and
sensing.

BACKGROUND OF THE INVENTION

The body uses physiological sensors for determining concentrations of
circulating substances, such as glucose. For example, it is well known that pancreatic
15 beta cells possess a glucose sensor, which reacts to increases in blood glucose, in
order to trigger insulin secretion. More recently, several researchers have identified a
glucose sensor that is triggered by a glucose gradient between the hepatic portal vein
and the hepatic artery (see, for example, the articles by Burcelin et al., cited
hereinbelow). This portoarterial glucose sensor is believed to be connected through
20 afferent hepatic branches of the vagus nerve to glucose-sensitive neurons in the lateral
hypothalamus and in the nucleus of the solitary tract. Activation of the portoarterial
glucose sensor, such as by food intake, stimulates hepatic glucose uptake, inhibits
food intake, inhibits counterregulation induced by hypoglycemic agents, and
stimulates glucose utilization by some insulin-sensitive tissues, such as muscle tissue.
25 Some published articles indicate that these processes appear not to be mediated by
insulin.

US Patent Application 09/734,358, which published as US Patent Application Publication 2002/0161414, and which is assigned to the assignee of the present patent application and is incorporated herein by reference, describes apparatus for treating a condition such as obesity. The apparatus includes a set of one or more electrodes, which are adapted to be applied to one or more respective sites in a vicinity of a body of a stomach of a patient. A control unit is adapted to drive the electrode set to apply to the body of the stomach a signal, configured such that application thereof increases a level of contraction of muscle tissue of the body of the stomach, and decreases a cross-sectional area of a portion of the body of the stomach for a substantially continuous period greater than about 3 seconds.

PCT Publication WO 02/082968 to Policker et al., which is assigned to the assignee of the present application and is incorporated herein by reference, describes a diet evaluation gastric apparatus, which detects when a patient swallows, and detects the type and amount of matter ingested. The apparatus includes electrodes adapted to be coupled to the fundus and antrum of the patient and to measure electrical and mechanical activity therein, and a control unit to analyze such electrical and mechanical activity and optionally apply electrical energy to modify the activity of tissue of the patient.

US Patent 5,231,988 to Wernicke et al., which is incorporated herein by reference, describes techniques for treating and controlling diabetes and other systemic pancreatic endocrine disorders attributable to abnormal levels of secretion of endogenous insulin. An electrical stimulator implanted into or worn external to the patient's body is adapted, when activated, to generate a programmable electrical waveform for application to electrodes implanted on the vagus nerve of the patient. The electrical waveform is programmed using parameter values selected to stimulate or inhibit the vagus nerve to modulate the electrical activity thereof to increase or decrease secretion of natural insulin by the patient's pancreas. The stimulator is selectively activated manually by the patient in response to direct measurement of

blood glucose or symptoms, or is activated automatically by programming the activation to occur at predetermined times and for predetermined intervals during the circadian cycle of the patient. Alternatively, the automatic activation is achieved using an implanted sensor to detect the blood glucose concentration, and is triggered
5 when the patient's blood glucose concentration exceeds or falls below a predetermined level depending on whether diabetes or hypoglycemia is being treated.

US Patents 5,188,104 and 5,263,480 to Wernicke et al., which are incorporated herein by reference, describe a method for stimulating the vagus nerve of a patient so as to alleviate an eating disorder.

10 US Patent 5,561,165 to Lutt et al., which is incorporated herein by reference, describes a method for increasing insulin responsiveness and improving glucose tolerance in a mammal, comprising administration of an effective amount of a cholinergic agonist. Pharmaceutical compositions are also described.

PCT Publication WO 01/76690 to Chen et al., which is incorporated herein by
15 reference, describes a method for regulating gastrointestinal action in a subject using a stimulatory electrode and a sensor to provide retrograde feedback control of electrical stimulation to the GI tract. The publication also describes a method for reducing weight in a subject, again using a stimulatory electrode and a sensor to provide retrograde feedback control of electrical stimulation to the stomach. The publication
20 further describes a method for stimulating the vagus nerve of a subject.

PCT Publication WO 02/04068 to Barrett et al., which is incorporated herein by reference, describes a method for treating patients for compulsive overeating, including stimulating left and right branches of the patient's vagus nerve simultaneously with electrical pulses in a predetermined sequence of a first period in
25 which pulses are applied continuously, alternating with a second period in which no pulses are applied. The electrical pulses are preferably applied to the vagus nerve at a supradiaphragmatic location.

US Patent 4,592,339 to Kuzmak et al., which is incorporated herein by reference, describes a gastric band for forming a stoma opening in a stomach for treating morbid obesity. The band is invasively placed around the stomach, and an expandable portion of the band is used to adjust the diameter of the stoma opening.

5 US Patents 5,449,368, 5,226,429, and 5,074,868 to Kuzmak, which are incorporated herein by reference, describe adjustable gastric bands. The size of the stoma opening of the bands can be adjusted by injecting into or removing fluid from an expandable section of the gastric bands.

10 US Patent 5,938,669 to Klaiber et al., which is incorporated herein by reference, describes an adjustable gastric band for contracting a patient's stomach in order to fight obesity. A gastric band of a known type, implanted around the stomach and including a cavity filled with liquid, is connected by a tube to a control box and a balancing reservoir which are implanted under the patient's skin. The box contains an electric pump and an electronic control unit capable of communicating by radio with a
15 monitor carried by the patient and with a controller intended for the doctor. The controller can operate the pump by remote control to transfer determined volumes of liquid in a closed circuit from the gastric band to the reservoir or vice versa, to adjust the diameter of a passage in the stomach. The monitor receives and signals alarms from the control box.

20 US Patent 6,067,991 to Forsell, which is incorporated herein by reference, describes an adjustable gastric band including an elongated non-inflatable restriction member, a forming device for forming the restriction member into at least a substantially closed loop around the stomach or the esophagus to define a restriction opening, and a post-operation non-invasive adjustment device for mechanically
25 adjusting the restriction member in the loop to change the size of the restriction opening.

US Patent 6,210,347 to Forsell, which is incorporated herein by reference, describes a food intake restriction device for forming a stoma opening in the stomach or esophagus of a patient.

5 US Patent to Forsell, which is incorporated herein by reference, describes a food intake restriction device for forming a stoma opening in the stomach or esophagus of a patient. The device comprises an elongated restriction member forming an expandable and contractible cavity formed into an at least substantially closed loop defining a restriction opening, the size of which is reduced upon expansion of the cavity and increased upon contraction of said cavity. A reservoir
10 containing a predetermined amount of hydraulic fluid and connected to the cavity of the restriction member, and a hydraulic operation device for distributing fluid from the reservoir to the cavity to expand the cavity and for distributing fluid from the cavity to the reservoir to contract the cavity, are also implanted in a patient with morbid obesity and operated from outside the patient's body in a non-invasive manner.

15 US Patent 6,453,907 to Forsell, which is incorporated herein by reference, describes an adjustable gastric band that includes an energy transmission device for wireless transmission of energy of a first form from outside the patient's body.

US Patent 6,454,699 to Forsell, which is incorporated herein by reference, describes a food intake restriction apparatus that includes a restriction device
20 implanted in a patient, which engages the stomach or esophagus to form an upper pouch and a restricted stoma opening in the stomach or esophagus. The restriction device optionally includes at least one implanted sensor for sensing at least one physical parameter of the patient, in which case the control device may control the restriction device in response to signals from the sensor.

25 US Patent Application Publication 2003/0066536 to Forsell, which is incorporated herein by reference, describes food intake restriction apparatus, including an operable restriction device implanted in a patient and engaging the stomach or

esophagus to form a restricted stoma opening in the stomach or esophagus. The apparatus includes a source of energy for energizing the restriction device, and a control device for releasing energy from the source of energy from outside the patient's body. The released energy is used in connection with the operation of the restriction device to vary the size of the stoma opening to allow or substantially prevent the passage of food therethrough. The restriction apparatus optionally includes a pressure sensor for directly or indirectly sensing the pressure in the stomach. The control device may control the restriction device in response to signals from the pressure sensor.

10 US Patent Application Publication 2001/0011543 to Forsell, which is incorporated herein by reference, describes apparatus for treating morbid obesity or heartburn and reflux disease, including an elongated restriction member formed in a substantially closed loop around a human's stomach or esophagus to form a stoma opening in the stomach or esophagus. The size of the stoma opening is adjustable by
15 an implanted adjustment device. A control device is utilized to control the adjustment device, in order to either reduce or enlarge the size of the stoma opening, for example in response to the time of the day. A sensor, such as a pressure or position sensor, is surgically implanted in the human's body so that the sensor may either directly or indirectly sense a physical parameter of the human, such as the pressure in the
20 stomach or the human's orientation with respect to the horizontal. If in response to sensing by the sensor it is determined by the control device that a significant change in the physical parameter has occurred, then the control device controls the adjustment device to either reduce or enlarge the size of the stoma opening.

US Patent 5,259,399 to Brown, which is incorporated herein by reference,
25 describes a method and apparatus for causing weight loss in obese patients by occupying a segment of the stomach volume using a variable volume bladder filled with fluid. The bladder is inserted into the upper part of the stomach including the fundus through a percutaneous endoscopic gastrostomy tube, which was non-

surgically placed to create a permanent channel to the stomach. The inserted bladder is filled and emptied using a filling system for pumping fluid in and out of the bladder according to a predetermined scheme. The filling system comprises a reversible pump, a two-way valve connected to the filling tube, an electronic control means for automatically controlling the action of the filling system, and a battery. The electronic control means is connected to a plurality of sensors placed on the patient's body to detect digestion cycle and hemodynamic parameters. The electronic control means collects information detected by the sensors, governs the filling system according to the obtained information and predetermined operation scheme, and records times and volumes of the fluid transferred through the two-way valve.

US Patent 6,514,718 to Heller et al., which is incorporated herein by reference, describes a small diameter flexible electrode designed for subcutaneous in vivo amperometric monitoring of glucose. The electrode is designed to allow "one-point" in vivo calibration, i.e., to have zero output current at zero glucose concentration, even in the presence of other electroreactive species of serum or blood. The electrode is preferably three or four-layered, with the layers serially deposited within a recess upon the tip of a polyamide insulated gold wire. A first glucose concentration-to-current transducing layer is overcoated with an electrically insulating and glucose flux limiting layer (second layer) on which, optionally, an immobilized interference-eliminating horseradish peroxidase based film is deposited (third layer). An outer (fourth) layer is biocompatible.

US Patent 5,368,028 to Palti, which is incorporated herein by reference, describes systems which utilize implanted chemo-sensitive living cells to monitor tissue or blood concentration levels of chemicals. The implanted cells produce a detectable electrical, optical or chemical signal in response to changes in concentration in surrounding medium. The signal is then detected and interpreted to give a reading indicative of blood concentration levels. Capsules containing chemo-sensitive cells and electrodes for detecting electrical activity are also disclosed.

INAMED Corporation (Santa Barbara, California) manufactures and markets the LAP-BAND® System, an FDA-approved adjustable and reversible gastric band for treatment of obesity.

5 The following articles, which are incorporated herein by reference, may be of interest:

Adachi A et al., "Convergence of hepatoportal glucose-sensitive afferent signals to glucose-sensitive units within the nucleus of the solitary tract," *Neurosci Lett* 46:215-218 (1984)

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15 Burcelin R et al., "GLUT4, AMP kinase, but not the insulin receptor, are required for hepatoportal glucose sensor-stimulated muscle glucose utilization," *J. Clin. Invest.* 111:1555-1562 (2003)

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20 Gardemann A et al., "Control of glucose balance in the perfused rat liver by the parasympathetic innervation," *Biol Chem Hoppe Seyler*. 367(7):559-66 (1986)

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Hartmann H et al., "Direct control of glycogen metabolism in the perfused rat liver by the sympathetic innervation," Eur J Biochem. 123(3):521-6 (1982).

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Shimazu T et al., "Reciprocal influences of the ventromedial and lateral hypothalamic nuclei on blood glucose level and liver glycogen content," *Nature* 210:1178-1179 (1966)

Shimazu T, "Glycogen synthetase activity in liver: regulation by the autonomic nerves," *Science* 156(779):1256-7 (1967)

Shimazu T et al., "Regulation of glycogen metabolism in liver by the autonomic nervous system. II. Neural control of glycogenolytic enzymes," *Biochim Biophys Acta.* 165(3):335-48 (1968)

Shimazu T et al., "Regulation of glycogen metabolism in liver by the autonomic nervous system. 3. Differential effects of sympathetic-nerve stimulation and of catecholamines on liver phosphorylase," *Biochim Biophys Acta.* 165(3):349-56 (1968)

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5 Shimizu N et al., "Functional correlations between lateral hypothalamic glucose-sensitive neurons and hepatic portal glucose-sensitive units in rat," *Brain Res*. 265:49-54 (1983)

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10 Watanabe Y et al, "Neural control of biosynthesis and secretion of serum transferring in perfused rat liver," *Biochem J*. 267(2):545-8 (1990)

Yamatani K et al., "Impaired vagus nerve-mediated control of insulin secretion in Wistar fatty rats," *Metabolism*. 47(10):1167-73 (1998)

15 Yoshimatsu H et al., "Lateral and ventromedial hypothalamic influences on hepatic autonomic nerve activity in the rat," *Brain Res Bull*. 21(2):239-44 (1988)

SUMMARY OF THE INVENTION

In some embodiments of the present invention, a method for treating a subject comprises applying an electrical current to the hepatic portal vein. Such stimulation generally increases uptake of blood glucose, e.g., by muscle, liver, and/or adipose tissue, thereby normalizing postprandial hyperglycemia, substantially lowering inter-meal blood glucose levels, and reducing food intake of the subject. The current is typically configured to stimulate afferent nerve terminals embedded in the wall of the hepatic portal vein. For some applications, the current is also configured to minimize artificially-induced activation of muscle tissue of the vein. The current is typically applied using one or more electrodes, which are either coupled to a surface of the hepatic portal vein, or implanted in the vein. Such electrical stimulation therefore is generally useful for treating subjects suffering from various medical conditions, such as obesity, diabetes, heart disease, and/or hypertension, or for preventively treating subjects considered at risk of developing such conditions.

In some embodiments of the present invention, a method for detecting eating by a subject comprises sensing a signal generated by a portoarterial glucose sensor of the subject. The signal is typically sensed by sensing electrical activity of the hepatic portal vein indicative of activity of afferent nerve fibers that innervate the vein. Such sensing is typically performed using one or more electrodes, which are either coupled to a surface of the hepatic portal vein, or implanted in the vein. Electrical activity of afferent nerve fibers that innervate the hepatic portal vein is generally correlated with the quantity of glucose recently absorbed by the small intestine during eating, and thus serves as an indicator of eating.

In some embodiments of the present invention, a method for detecting eating by a subject comprises sensing changes in blood glucose, carbohydrate, fat, or protein concentration in blood in the hepatic portal vein. Such changes are generally correlated with the quantity of glucose, carbohydrate, fat, or protein recently absorbed by the small intestine during eating. For some applications, such changes are detected

by measuring hepatic portal blood flow, which tends to increase corresponding to increases in postprandial portal blood glucose, carbohydrate, fat, or protein levels. The changes in blood flow may be detected using a flow meter attached to the portal vein, such as a pulsed Doppler ultrasonic flow meter, or a meter that utilizes the thermodilution principle. Alternatively, the changes are measured by measuring changes in impedance between electrodes placed on the external surface of the portal vein. Further alternatively, the changes are measured using chemical or non-chemical blood analysis techniques, such as: (a) near-infrared or infrared absorption spectroscopy, or (b) a laser transducer implanted on the portal vein together with an acoustic sensor that measures changes in acoustic reflections from the blood, which reflections are correlated with blood glucose level.

In some embodiments of the present invention, hepatic portal vein stimulation is applied responsive to detection of eating by the subject. For some applications, such detection is performed using the techniques described hereinabove for sensing a portoarterial glucose sensor signal and/or sensing hepatic portal blood glucose, carbohydrate, fat, or protein concentrations. Alternatively, such detection is performed using techniques described in the above-mentioned '414 patent application publication and/or '968 PCT publication, or using techniques known in the art. In other embodiments, hepatic portal vein stimulation is applied generally constantly, not responsive to detection of eating. Alternatively, the stimulation is applied periodically, such as during certain times of day or night.

There is therefore provided, in accordance with an embodiment of the present invention, a method for treating a subject, including:

applying an electrical current to a hepatic portal vein of the subject; and

configuring the current so as to increase glucose uptake by tissue of the subject.

There is also provided, in accordance with an embodiment of the present invention, a method for detecting eating by a subject, including:

sensing an electrical signal generated by a portoarterial glucose sensor of the subject; and

analyzing the signal in order to detect the eating.

For some applications, sensing the signal includes sensing electrical activity of a hepatic portal vein of the subject. Alternatively or additionally, sensing the signal includes sensing electrical activity of a hepatic branch of a vagus nerve of the subject.

There is further provided, in accordance with an embodiment of the present invention, a method for detecting eating by a subject, including:

measuring a concentration of glucose, carbohydrate, fat, or protein in a hepatic portal vein of the subject; and

analyzing the concentration in order to detect the eating.

For some applications, measuring the concentration includes measuring a rate of blood flow within the hepatic portal vein. For some applications, analyzing the concentration includes analyzing the concentration in order to detect a composition of food eaten by the subject.

The present invention will be more fully understood from the following detailed description of embodiments thereof, taken together with the drawings, in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic illustration of a hepatic interface system applied to a human liver, in accordance with an embodiment of the present invention; and

Fig. 2 is a schematic block diagram of another hepatic interface system applied to a nerve of a subject, in accordance with an embodiment of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Fig. 1 is a schematic illustration of a hepatic interface system 10 applied to a human liver 20, in accordance with an embodiment of the present invention. A hepatic portal vein 22 carries blood to liver 20 from a digestive tract 24, including a small intestine 26 and a stomach 28. A hepatic artery 30 brings oxygen-rich blood to liver 20. Portal vein 22 and hepatic artery 30 enter liver 20 through a hepatic hilum 32.

System 10 comprises an implantable or external control unit 42 coupled to an electrode device 44. Electrode device 44 typically comprises one or more electrodes that are either implanted in portal vein 22, or applied to an external surface of portal vein 22. In the latter case, the electrodes typically comprise cuff electrodes. Electrode device 44 is generally applied to portal vein 22 in a vicinity of hepatic hilum 32.

In an embodiment of the present invention, control unit 42 drives electrode device 44 to apply an electrical current to portal vein 22. The control unit typically configures the current to stimulate afferent nerve terminals embedded in the wall of portal vein 22. Additionally, the control unit typically configures the current to generally minimize artificially-induced activation of muscle tissue of the vein. Depending on the specific design of the electrodes and electrode device 44, appropriate parameters of the current may include a frequency of between about 5 Hz and about 100 Hz, and an amplitude of between about 1 and about 15 milliamps.

Such electrical stimulation generally activates the portoarterial glucose sensor, in a manner similar to the natural activation of this physiological sensor by a positive glucose gradient between portal vein 22 and hepatic artery 30, as described hereinabove. Such stimulation thus generally increases uptake of blood glucose, e.g., by muscle, liver, and/or adipose tissue, thereby normalizing postprandial hyperglycemia, substantially lowering inter-meal blood glucose levels, and/or

reducing food intake of the subject. Such stimulation therefore is generally useful for treating subjects suffering from various medical conditions, such as obesity, diabetes, and/or heart disease, or for preventively treating subjects considered at risk of developing such conditions.

5 In an embodiment of the present invention, control unit 42 uses electrode device 44 to sense electrical changes in activity of portal vein 22. Such sensing is typically configured to sense electrical activity indicative of activity of afferent nerve fibers that innervate portal vein 22. Such sensing is thus generally indicative of the level of activation of the portoarterial glucose sensor of the subject, and is therefore
10 generally correlated with the quantity of glucose recently absorbed by the small intestine during eating. In this embodiment, therefore, system 10 serves as an indicator of eating. For some applications, a type of electrical change which is detected is a decrease in electrical activity in the portal vein. Other changes include, alternatively or additionally, increases in electrical activity, changes in heights of
15 different measured peaks, and/or changes in the relative timing of different peaks in the sensed electrical activity.

In an embodiment of the present invention, system 10 alternatively or additionally comprises a food intake detection device 50, which is coupled to portal vein 22. For some applications, food intake detection device 50 comprises a blood
20 flow sensor, which is adapted to detect a rate of blood flow in portal vein 22. Increased portal blood flow is generally indicative of elevated postprandial portal blood glucose, carbohydrate, fat, or protein levels, and thus indicates the quantity of such products recently absorbed by small intestine 26 during eating. For example, the blood flow sensor may comprise an implantable blood flow meter, e.g., a pulsed
25 Doppler ultrasonic flow meter, or a meter that utilizes the thermodilution principle. Alternatively, the blood flow sensor comprises one or more electrodes adapted to measure changes in impedance between the electrodes, which changes are indicative of stretching of portal vein 22 caused by increased portal blood flow. For such

applications, detection device 50 may comprise the electrodes of electrode device 44, or, alternatively, separate electrodes. In an embodiment, detection device 50 uses chemical or non-chemical blood analysis techniques to directly detect glucose levels. For example, the glucose detection device may utilize: (a) near-infrared or infrared
5 absorption spectroscopy, or (b) a laser transducer implanted on the portal vein together with an acoustic sensor that measures changes in acoustic reflections from the blood, which reflections are correlated with blood glucose level. Alternatively, the glucose detection device uses more invasive techniques, such as those described in the above-mentioned US Patent 6,514,718 to Heller et al. or the above-mentioned US
10 Patent 5,368,028 to Palti.

In an embodiment of the present invention, control unit 42 is configured to drive electrode device 44 to stimulate portal vein 22 responsive to detection of eating by the subject. For some applications, such eating detection is performed using one or more of the techniques described hereinabove. Alternatively, such detection is
15 performed using techniques described in the above-mentioned '414 patent application publication, the above-mentioned '968 PCT publication, the above-mentioned US Provisional Patent Application, entitled, "Gastrointestinal methods and apparatus for use in treating disorders," or using techniques known in the art. In another embodiment of the present invention, control unit 42 is configured to drive electrode
20 device 44 to stimulate portal vein 22 generally constantly, not responsive to detection of eating. Alternatively, the stimulation is applied periodically, such as during certain times of day or night, or in response to a command from the subject.

In an embodiment of the present invention, system 10 comprises an appetite control device 52. Upon detection of eating using the techniques described herein,
25 control unit 42 drives appetite control device 52 to reduce an appetite of the subject, such as by increasing a sensation of satiety. For example, appetite control device 52 may utilize appetite reduction techniques (a) described in the above-mentioned '414 patent application publication and/or the above-mentioned '968 PCT publication, (b)

described in the gastric band or balloon patents mentioned in the Background of the Invention, and/or (c) known in the art (e.g., by administration of an appetite suppressing medication). Alternatively or additionally, upon detection of eating using the techniques described herein, system 10 performs the colonic stimulation techniques described in the above-mentioned US Provisional Patent Application, entitled, "Gastrointestinal methods and apparatus for use in treating disorders."

In an embodiment of the present invention, upon detection of eating using the techniques described herein, control unit 42 drives an internal or implanted device to increase insulin levels in blood of the subject. For example, devices appropriate for increasing insulin levels include, but are not limited to:

- insulin pumps, as known in the art;
- devices for increasing insulin secretion by direct or indirect stimulation of the pancreas, such as those described in PCT Publication WO 01/91854 to Harel et al.; PCT Patent Publication WO 03/45493 to Harel et al.; and/or US Patent 5,919,216 to Houben et al., all of which are incorporated herein by reference; and
- devices for modulating insulin secretion by direct stimulation of the vagus nerve, such as those described in the above-referenced US Patents 5,188,104, 5,231,988, and/or 5,263,480 to Wernicke et al.

Reference is now made to Fig. 2, which is a schematic block diagram of a hepatic interface system 100 applied to a nerve 102 of a subject, in accordance with an embodiment of the present invention. System 100 is generally similar to hepatic interface system 10, as described hereinabove with reference to Fig. 1, except for differences described hereinbelow. System 100 comprises a control unit 142, and, for some applications, an appetite control device 152. In addition, system 100 comprises an electrode device 144, adapted to be coupled to nerve 102. Nerve 102 conducts afferent impulses generated by the portoarterial glucose sensor. For example, nerve

102 may comprise a vagus nerve of the subject, or a branch of the vagus nerve, such as a hepatic branch of the vagus nerve. To detect activation of the portoarterial glucose sensor, control unit 142 senses electrical activity of nerve 102, using, for example, techniques described hereinabove with reference to Fig. 1, *mutatis mutandis*.

5 To effect appetite suppression, control unit 142 drives electrode device 144 to apply a current to nerve 102, with parameters generally configured to mimic the natural afferent nerve signals generated by the portoarterial glucose sensor. For example, the current may be configured to be such as to excite affected tissue, or to inhibit affected tissue.

10 It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art
15 upon reading the foregoing description.

CLAIMS

1. A method for treating a subject, comprising:
applying an electrical current to a hepatic portal vein of the subject; and
configuring the current so as to increase glucose uptake by tissue of the
5 subject.
2. A method for detecting eating by a subject, comprising:
sensing an electrical signal generated by a portoarterial glucose sensor
of the subject; and
analyzing the signal in order to detect the eating.
- 10 3. The method according to claim 2, wherein sensing the signal comprises
sensing electrical activity of a hepatic portal vein of the subject.
4. The method according to claim 2, wherein sensing the signal comprises
sensing electrical activity of a hepatic branch of a vagus nerve of the subject.
5. A method for detecting eating by a subject, comprising:
15 measuring a concentration of glucose, carbohydrate, fat, or protein in a
hepatic portal vein of the subject; and
analyzing the concentration in order to detect the eating.
6. The method according to claim 5, wherein measuring the concentration
comprises measuring a rate of blood flow within the hepatic portal vein.
- 20 7. The method according to claim 5, wherein analyzing the concentration
comprises analyzing the concentration in order to detect a composition of food eaten
by the subject.

FIG. 1

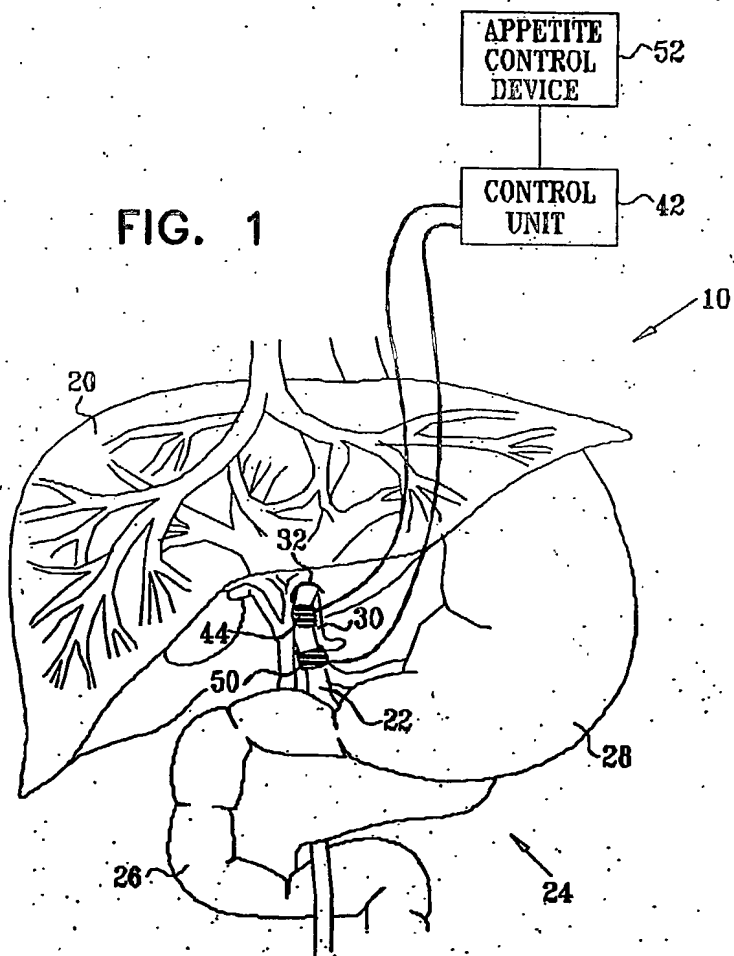
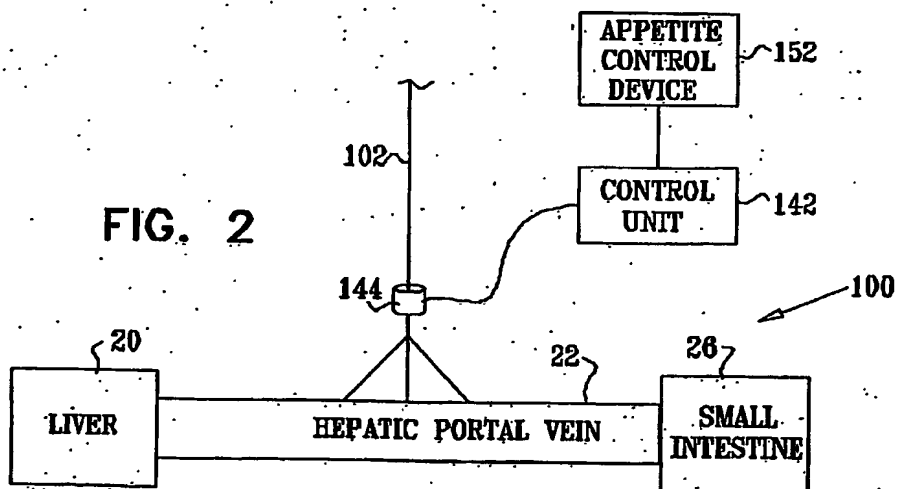


FIG. 2



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